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Aggravation of Anemia by Helico Bacter Pylori Infection in Maintenance Hemodialysis Patients

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Abstract: To elucidate whether and how in patients on maintenance hemodialysis (HD), infection of *H. pylori* intensifies the anemia, a cross-sectional study that was conducted on 39 patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis treatment who had various upper gastrointestinal complaints consisting of epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating and belching. Mean ages of patients were 46(±18) years. The dialysis duration was 30±(35) months (median: 18 months). Mean±SD of hemoglobin and hematocrit level of all patients were 9±2 g/dl and 28±6%. The value of serum helicobacter pylori (*H. Pylori*) specific IgG antibody titers of all patients was 7.6 (±9.9)u/ml (median:2 u/ml). In this study non significant difference of *H. Pylori*-IgG antibody level between males and females or diabetic and non-diabetic hemodialysis patients were seen, and a significant inverse correlation of *H. Pylori*-IgG antibody level with serum hemoglobin and hematocrit in male hemodialysis patients and a significant inverse correlation of *H. Pylori*-IgG antibody level with serum iron were found. Also non significant correlation of serum *H. Pylori*-IgG antibody level with Hgb, Hct and serum iron in all patients, female, non diabetics and diabetic HD groups were found. In hemodialysis patients an inverse correlation between *H. pylori* infection with hemoglobin and hematocrit level as well as with serum iron, implies more attention to *H. pylori* infection in these patients and aggravation of anemia with *H. pylori* infection needs aggressive treatment of *H. pylori* infection in these patients.

Key words: Hemodialysis, end-stage renal failure, anemia, helicobacter pylori infection

Introduction

Anemia is a consistent finding in chronic renal disease, affecting up to 90% of patients, and the central role of anaemia in the development of cardiovascular dysfunction is now well established, anemia of end-stage renal disease can be managed relatively successfully by recombinant human erythropoietin (Nasri, 2003; Baradaran and Nasri, 2005). Iron administration plays a central role in enhancing anaemia responsiveness to EPO and serum ferritin concentration is a commonly used marker of iron status in maintenance dialysis patients (Kalantar-Zadeh *et al.*, 2003). Helicobacter pylori (*H. pylori*) is a spiral-shaped bacterium that causes chronic infection in human stomachs, and often leads to gastritis and peptic ulcers (Blaser, 1992; Baradaran and Nasri, 2005). In dialysis patients chronic infections induce overproduction of pro-inflammatory substances, inflammation has been associated with cachexia and anorexia (Kahraman *et al.*, 2005). Infection with *H. pylori* is also associated with anorexia, inflammation, and malnutrition in dialysis patients (Nardone *et al.*, 2005). Malnutrition is a relevant risk factor for mortality for patients on maintenance hemodialysis treatment (Leavy *et al.*, 2001). Studies concerning the association of *H. pylori* infection with malnutrition in hemodialysis population showed various results. Previously we showed the inverse association

of *H. pylori* infection with serum albumin of hemodialysis patients (Baradaran and Nasri, 2005) In this study aimed to elucidate whether and how in patients with uremia on maintenance hemodialysis, infection of *H. pylori* intensifies the anemia of hemodialysis patients.

Materials and Methods

This is a cross-sectional study that was conducted on patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes. All study patients had various upper gastrointestinal complaints consisting of epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating and belching. Exclusion criteria for patients were using of H₂ proton pump inhibitors and antibiotics or taking aluminum hydroxide jells as well as active or chronic infection before the study. Blood samples were drawn after an overnight fast. Each blood samples were centrifuged within 15 minutes of venepuncture. Serum helicobacter pylori specific IgG antibody titers (titer >10 U/ml was interpreted as positive according to the manufacturer's instructions) was measured by enzyme-linked immunosorbent assay (ELISA) method using Trinity Biotech Kits (USA). Intact serum PTH (iPTH) was measured by the radioimmunoassay (RIA) method using DSL-8000kits of USA (normal range of values is

10-65 pg/ml). Also peripheral venous blood samples were collected for biochemical analysis including serum post and predialysis blood urea nitrogen (BUN), Cholesterol (chol), triglyceride (Tg), albumin (Alb), C-reactive protein (CRP), serum phosphorus (p) and calcium (Ca) were measured using standard methods. Levels of serum iron, total iron binding capacity (TIBC) and serum ferritin (by RIA method) were measured using standard kits. For patients also complete blood count containing hemoglobin (Hgb) and hematocrit (Hct) were measured using Sysmex-KX-21N Cell counter. For the efficacy (adequacy) of hemodialysis the urea reduction rate (URR) was calculated from pre- and post-blood urea nitrogen (BUN) data. Body mass index (BMI) calculated using the standard formula (post dialyzed weight in kilograms/height in square meters; kg/m^2). Duration and doses of hemodialysis treatment were calculated from patients' records. The duration of each hemodialysis session was four hours. For statistical analysis, the data are expressed as the Mean \pm SD and median values. Statistical correlations were assessed using the partial correlation test. Comparison between the groups was done using Student's t-test. Statistical analysis was performed on all hemodialysis (HD) patients, females, males, diabetics and non diabetic groups separately. All statistical analyzes were performed using SPSS (version 11.5.00). Statistical significance was determined at a p-value lower than 0.05.

Results

The study was carried on 39 (F = 15 M = 24) stable hemodialysis (HD) (diabetic = 12 non-diabetics = 27) patients. Table 1 shows patients' data. Mean ages of patients were 46 ± 18 years. The length of the time patients had been on hemodialysis was 30 ± 35 months (median: 18 months). Mean \pm SD of hemoglobin and hematocrit level of all patients were 9 ± 2 g/dl (median: 9g/dl), and $28 \pm 6\%$ (median: 29%) respectively. The value of serum helicobacter pylori (*H. Pylori*) specific IgG antibody titers of all patients was 7.6 ± 9.9 u/ml (median: 2 u/ml). The value of serum helicobacter pylori (*H. Pylori*) specific IgG antibody titers in the female and male groups were 5.9 ± 8 u/ml (median :2 u/ml) and $8.7 (\pm 10.9)$ u/ml (median :2 u/ml) respectively. In this study no significant difference of *H. Pylori*-IgG antibody level between males and females or diabetic and non-diabetic hemodialysis patients were found (p N.S.). In this study in male group a significant inverse correlation of logarithm of *H. Pylori*-IgG antibody level with serum hemoglobin ($r = -0.56$, $p = 0.035$) and hematocrit ($r = -0.63$, $p = 0.015$) were seen (adjusted for age, duration and doses of dialysis, URR, WBC count, serum iPTH, CRP, Tg, Phosphorus and serum iron for two above correlations) were seen. In this group also a significant inverse correlation of logarithm of *H. Pylori*-IgG antibody

level with serum iron ($r = -0.61$, $p = 0.044$; Fig. 1) (adjusted for age, duration and doses of dialysis, URR, WBC count, BMI, Chol, serum iPTH, Ca, CRP, Tg and serum phosphorus). No significant correlation of serum *H. Pylori*-IgG antibody level with Hgb, Hct and serum Iron in all patients, female, non diabetics and diabetic HD group were seen (P N.S.). In this study no significant correlation of serum *H. Pylori*-IgG antibody level with serum ferritin in all groups was found.

Discussion

Principal findings of the present study were, non significant difference of *H. Pylori*-IgG antibody level between males and females or diabetic and non-diabetic hemodialysis patients and a significant inverse correlation of *H. Pylori*-IgG antibody level with serum hemoglobin and hematocrit in male hemodialysis patients and a significant inverse correlation of *H. Pylori*-IgG antibody level with serum iron. We also found non significant correlation of serum *H. Pylori*-IgG antibody level with Hgb, Hct and serum Iron in all patients, female, non diabetics and diabetic HD groups and also non significant correlation of serum *H. Pylori*-IgG antibody level with serum ferritin in all groups were found. Recent reports support the possible association between Helicobacter pylori infection and iron deficiency anemia, specially an association between Helicobacter pylori infection and iron deficiency anemia has been reported in children, and it has been proposed that *H. pylori* infection needs to be eradicated to treat absolutely iron deficiency anemia (IDA) (10,11). In a study on 140 children aged 6--16 years (median 9.5 years) who received anti-*H. pylori* combination therapy, Kureki *et al.* (2005) found that hemoglobin and MCV values rose significantly compared with baseline values after *H. pylori* eradication without iron supplementation in children with iron deficiency anemia (IDA) and ferritin values increased significantly after *H. pylori* eradication in children with iron deficiency. They concluded that complete recovery of iron deficiency and iron deficiency anemia can be achieved with *H. pylori* eradication without iron supplementation in children with *H. pylori* infection (Kureki *et al.*, 2005). In the study conducted by Choe *et al.*, 2001 on 440 regular high school students and 220 athletes of a physical education high school, showed that, adolescent female athletes may have development of *H. pylori* -associated IDA, which can be managed by *H. pylori* eradication. (Choe *et al.*, 2001). Hacıhanefioglu *et al.*, 2004 carried-out a study on fourteen women with iron deficiency anemia with mean age of 36.4 years which one of them received iron supplementation. After examinations including upper and lower gastrointestinal endoscopy which revealed any gastrointestinal bleeding sites in all patients and g astric biopsies for diagnosing of Hp infection found serum hemoglobin, iron and transferrin saturations of

Table 1: Mean±SD, Minimum and Maximum of age, duration and dosage hemodialysis and also laboratory results of all hemodialysis patients

patients n=39	Mean±SD	Median
Age years	18±46	42
DH* months	35±30	18
Dialysis dose sessions	381±279	156
BMI kg/m ²	21.6±4.3	21
H. Pylori-IgG u/ml	7.6±9.9	2
Tg mg/dl	130±95	94
Chol mg/dl	38±116	110
Hgb g/dl	2±8.9	9
Alb g/l	0.5±3.8	4
URR %	8±58	58
CRP mg/l	6.7±8.8	6
Hct %	6±28	29
iPTHpg/ml	434±455	309
Ca mg/dl	7.7 ±1	8
Pmg/dl	6.4±1.9	6.4
Ferritin ng/dl	519±299	426
Iron µg/dl	350±454	69
TIBCµg/dl	968±562	1059

*duration of hemodialysis

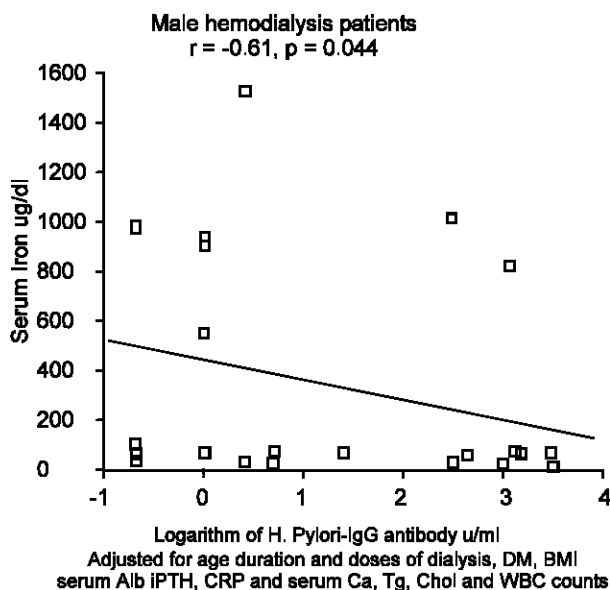


Fig. 1: Significant inverse correlation of logarithm of *H. Pylori*-IgG antibody level with serum iron

the patients were increased at 20-24 weeks of follow-up after the eradication therapy for *h. pylori*. Serum ferritin levels were not found to be increased. They concluded that infection may be involved in cases of iron deficiency anemia of unknown origin, and the eradication of the infection may improve blood parameters other than serum ferritin levels (Hacihanefioglu *et al.*, 2004). Also Valiyaveettil *et al.*, 2005 in a study on 52 patients with iron-deficiency anemia, showed in patients with iron-

deficiency anemia, presence of *H. pylori* infection is associated with a poorer response to oral iron therapy, which improves with treatment for *H. pylori* infection (Valiyaveettil *et al.*, 2005). Indeed about 35% of iron deficiency anemia cases remain unexplained after a gastrointestinal evaluation. *H. pylori* infection and chronic gastritis, especially atrophic gastritis, are significantly associated with unexplained iron deficiency anemia. Relationships between *H. pylori*-associated chronic gastritis and unexplained iron deficiency anemia in these conditions should be considered (Nahon *et al.*, 2003). Taken together, In the studies mentioned above the correlation of *H. pylori* infection with IDA was considered. We showed that presence of *H. pylori* infection is associated with a poorer response to oral iron therapy, which improves with treatment for *H. pylori* infection. In patients on maintenance hemodialysis we could show an inverse correlation between *H. pylori* infection with hemoglobin and hematocrit level as well as with serum iron, implies more attention to *H. pylori* infection in these patients that one their important problem is anemia, hence aggravation of anemia with *H. pylori* infection needs aggressive treatment of *H. pylori* infection in these patients.

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